

## Altered microRNA expression profiles in large offspring syndrome and Beckwith-Wiedemann syndrome (2019)

Yahan Li, Darren Erich Hagen, Tieming Ji, Mohammed Reza Bakhtiarizadeh, Whitney M. Frederic, Emily M. Traxler, Jennifer M. Kalish, Rocío Melissa Rivera

### Background

Beckwith-Wiedemann Syndrome (BWS) is an overgrowth disorder whose features include both generalized overgrowth and overgrowth of specific organs including the tongue, liver, kidney, limbs, and an increased tumor risk. In addition to studying patients with the disorder, scientists are also developing animal models of syndromes like BWS so that they can study more details about early development that cannot be easily studied in humans.

In the case of BWS, one animal model that is being studied is in cows and is called Large Offspring Syndrome (LOS). LOS has many similar features to BWS and is caused by epigenetic changes similar to BWS. By studying more about LOS, we can better understand BWS – how it arises, how it differs between individuals and possibly how to treat it effectively.

We understand that BWS arises due to DNA being ‘marked’ differently at a region on chromosome 11, in a process called methylation. In BWS, different levels of methylation leads to different levels of gene expression, resulting in the associated characteristics.

However, studies have shown that LOS cattle have large-scale changes to gene expression that cannot be explained by differences in methylation alone. These widespread changes point to the possibility of altered expression of microRNA molecules (miRNAs). miRNAs are small RNA molecules that regulate gene expression, typically turning on or off multiple genes.

### Purpose

To determine whether miRNA expression is being misregulated in LOS and BWS.

### Findings

- miRNA expression is misregulated in both LOS and BWS with some common themes or pathways.
- The pathways that are misregulated due to different miRNA expression are related to cell cycles, cell growth, cell division, control of organ size and other functions that link to the overgrowth symptoms and tumor growth in BWS.
- Methylation beyond the BWS region may be the cause of this misregulation of miRNA, hence playing a larger role in affecting gene expression.

### Key Points

- Different miRNA expression is a key part of BWS and its animal model, LOS.
- This different miRNA expression affects reaction pathways beyond those involving the genes from chromosome 11 that are known to be linked to BWS.

### Reference

Li Y et al. Altered microRNA expression profiles in large offspring syndrome and Beckwith-Wiedemann syndrome. *Epigenetics*. 2019;14(9): 850-876. PubMed PMID: 31144574